# PROTEIN DISORDERS

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# 4- Alpha-1 antitrypsin deficiency (AATD)

It is an autosomal recessive inheritance disorder that causes a deficiency or absence of the alpha-1 antitrypsin (AAT) protein in the blood. AAT is made in the liver and sent through the bloodstream to the lungs, to protect the lungs from damage. Having low levels of ATT (or no ATT) can allow the lungs to become damaged, making breathing hard. Age of onset and severity of AATD can vary based on how much ATT is affected.

# Signs and Symptoms:

Very frequent symptoms: Emphysema and hepatic failure. Frequent symptoms: Jaundice, hepatitis, and hepatomegaly. Occasional symptoms: Cirrhosis, nephrotic syndrome, chronic obstructive pulmonary disease and Dyspnea.

# Causes:

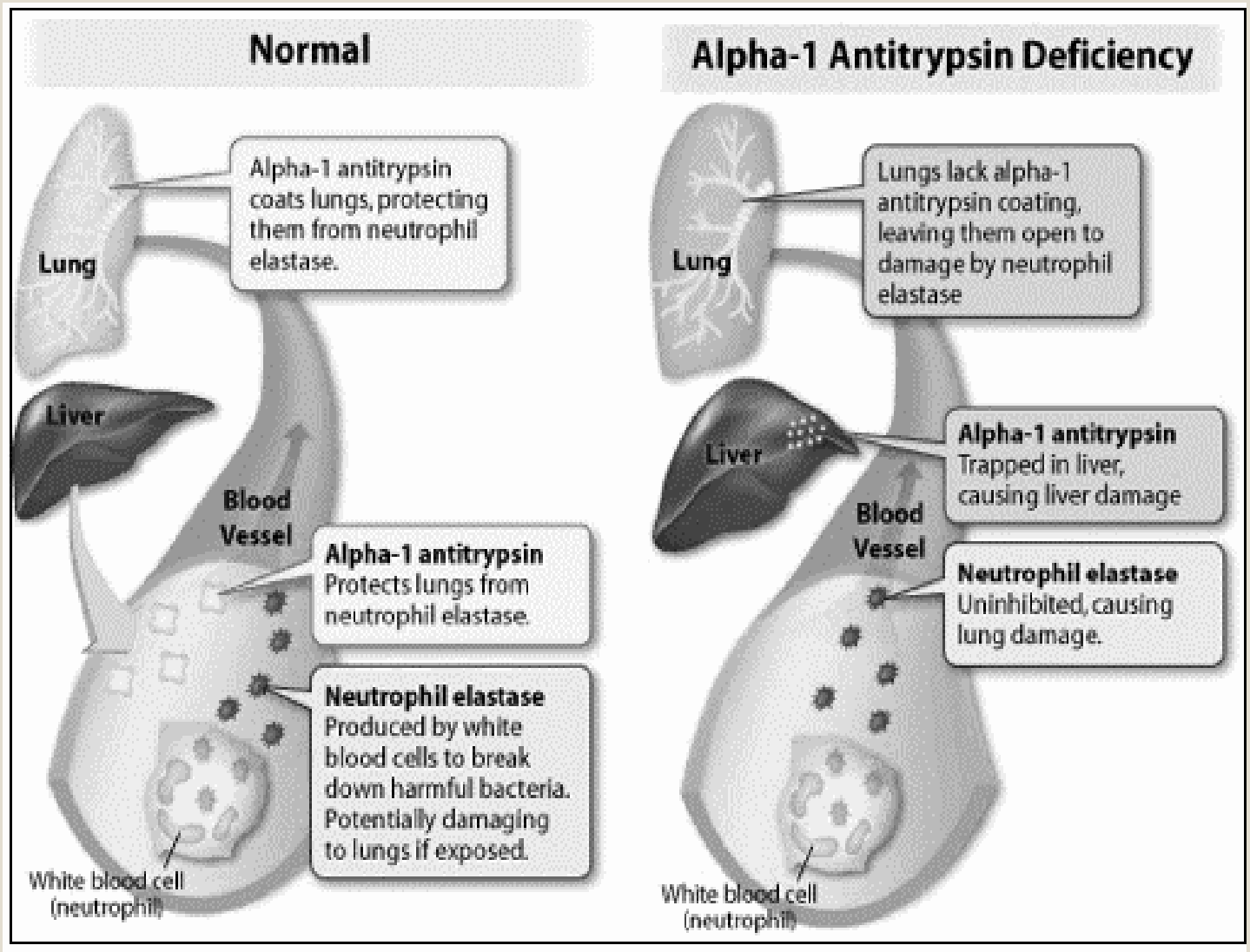
Alpha-1 antitrypsin deficiency is caused by mutations in the SERPINA1 gene. This gene gives the body instructions to make a protein called AAT, which protects the body from an enzyme called neutrophil elastase that helps the body fight infections, but it can also attack healthy tissues (especially the lungs) if not controlled by AAT.

Mutations that cause AAT can cause a deficiency or absence of AAT, or a form of AAT that does not work well. This allows neutrophil elastase to destroy lung tissue, causing lung disease. In addition, abnormal AAT can build up in the liver and cause damage to the liver. The severity of AATD may also be worsened by environmental factors such as exposure to tobacco smoke, dust, and chemicals.

# Treatment:

- Treatment of AATD depends on the symptoms and severity in each person. Chronic obstructive respiratory disease (COPD) and other related lung diseases are typically treated with standard therapy. Bronchodilators and inhaled steroids can help open the airways and make breathing easier.

- Intravenous augmentation therapy (regular infusion of purified, human AAT to increase AAT concentrations) has been recommended for people with established fixed airflow obstruction (determined by a specific lung function test). This therapy raises the level of the AAT protein in the blood and lungs. Lung transplantation may be an appropriate option for people with end-stage lung disease. also liver transplantation is the definitive treatment for advanced liver disease.


Normal
Alpha-1 Antitrypsin Deficiency
Lung
Alpha-1 antitrypsin coats lungs, protecting them from neutrophil elastase.
Liver
Blood Vessel
Alpha-1 antitrypsin
Protects lungs from neutrophil elastase.
Neutrophil elastase
Produced by white blood cells to break down harmful bacteria. Potentially damaging to lungs if exposed.
White blood cell (neutrophil)
Lung
Lungs lack alpha-1 antitrypsin coating, leaving them open to damage by neutrophil elastase
Liver
Alpha-1 antitrypsin
Trapped in liver, causing liver damage
Blood Vessel
Neutrophil elastase
Uninhibited, causing lung damage.
White blood cell (neutrophil)

## 5- Mannose-binding lectin protein deficiency

- Mannose-binding lectin (MBL) deficiency results in a decreased amount of a specific protein involved in the immune system. It was originally thought that MBL deficiency resulted in an increased susceptibility to infections. However, low levels of this protein have been found in many healthy people. MBL deficiency is more likely to be associated with infections in toddlers and those who have a weakened immune system (immune-compromised), including those with an underlying medical condition cancer patients undergoing chemotherapy, and organ-transplant patients.

MBL deficiency is caused by changes in the MBL2 gene. However, it is important to note that changes in this gene are very common in the general population.

# Treatment:

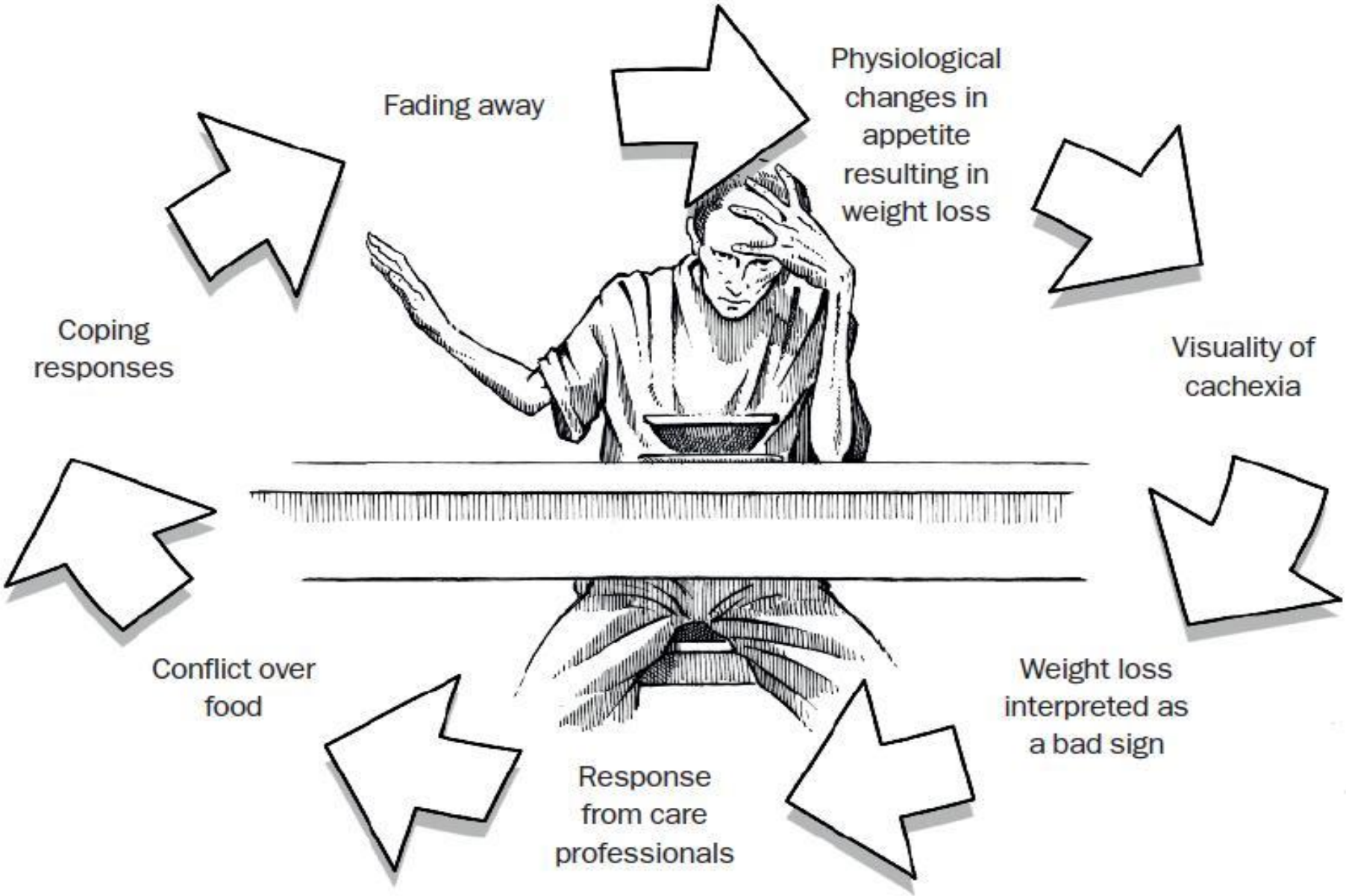
Treatment for individuals with recurrent infections and MBL deficiency may include antibiotics to treat bacterial infections and regular vaccinations. Prophylactic antibiotics may be indicated in some cases.

## 6- Cachexia

Cachexia is a condition that involves protein deficiency, depletion of skeletal muscle and an increased rate of protein degradation.

Cachexia causes weight loss and mortality and is associated with cancer, AIDS, chronic kidney failure, heart disease, chronic obstructive pulmonary disease and rheumatoid arthritis.

Patients with malignant cancer of the stomach, colon, liver, biliary tract and pancreas experience under-nutrition from reduced intake of protein, calories and micronutrients, and have fatigue and a negative nitrogen balance as a result of loss of muscle mass from cachexia.

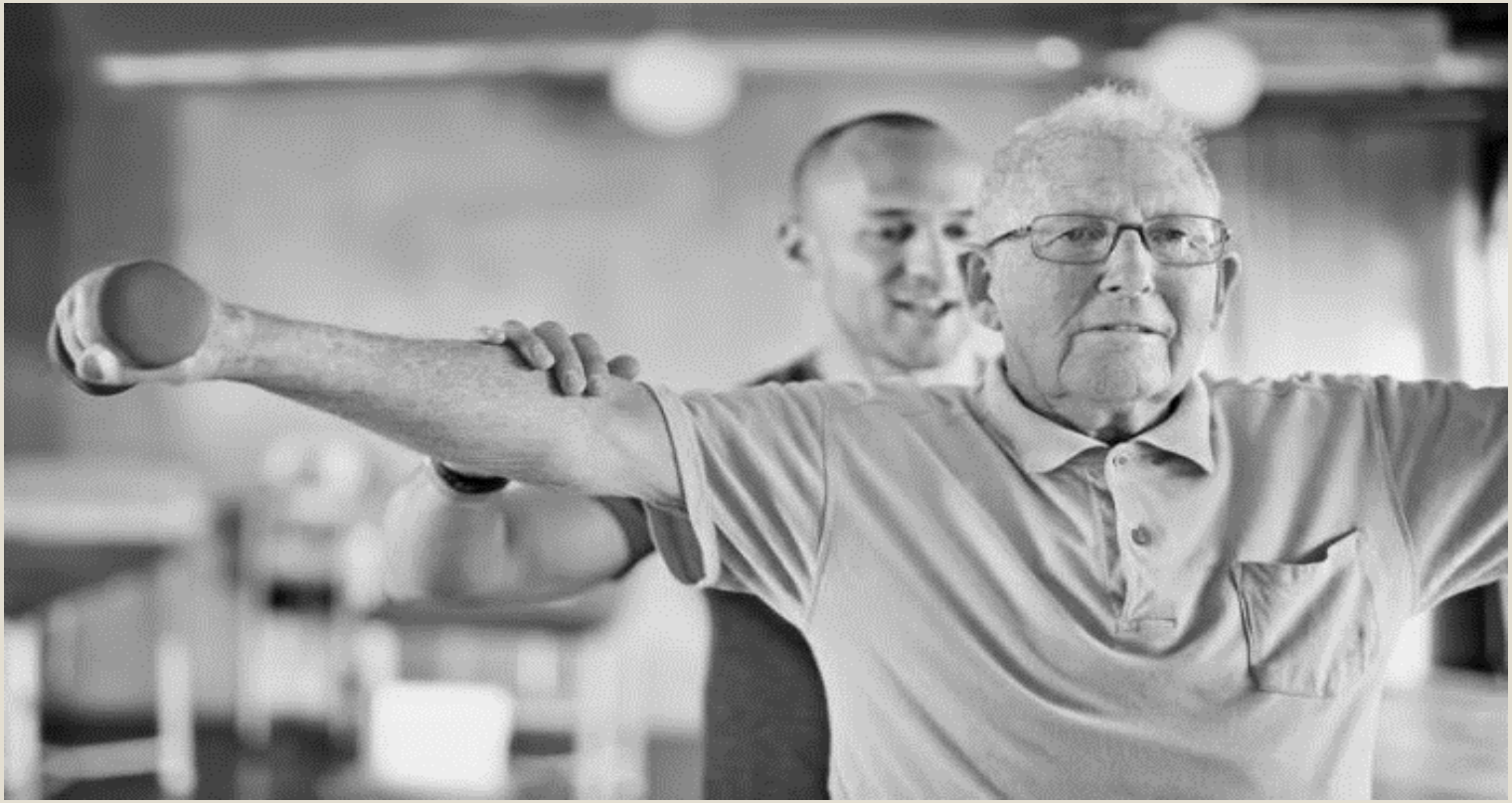

Fading away
Physiological changes in appetite resulting in weight loss
Coping responses
Visuality of cachexia
Conflict over food
Weight loss interpreted as a bad sign
Response from care professionals

# Treatment:

- Treatments for cachexia can include medications to reduce the cytokines in the body, stimulate appetite, or block hormones associated with causing cachexia.

- Examples of appetite stimulants include dronabinol and megesterol acetate. Corticosteroids, such as dexamethasone, methylprednisolone, and prednisolone, also stimulate appetite.

- However, dietary changes are rarely enough to reverse the incidences of the muscle wasting associated with cachexia . Muscle mass can be built up through exercise. If physically able, a person may try resistance training by lifting weights, using resistance bands, or using a person's body weight. Sometimes, growth hormone, such as Serostim or Norditropin FlexPro may be used.



# Foods That Cure Protein Deficiencies

- Red Meat such as beef, contains high amounts of dietary protein that can help correct protein deficiencies. Meat and other animal-based foods contain high-quality, or complete, proteins. Complete proteins provide bodies with all essential amino acids
- Chicken is a complete protein that is typically low in fat, depending on how it's prepared. Consuming chicken can help prevent or reverse dietary protein deficiencies.
- Fish is high in protein, low in fat and contains beneficial omega-3 fatty acids. However, pregnant women, women who may become pregnant, breast-feeding women and children should avoid consumption of certain types of fish due to high levels of mercury.

- Eggs contain high-quality protein that can help cure protein deficiencies. Thoroughly cook eggs until they are not runny, to prevent salmonella food poisoning. One large egg provides about six grams of complete protein.

- Soy although most plant-based foods contain incomplete proteins, soy is an exception and contains all essential amino acids.

- Legumes such as kidney beans, pinto beans, black beans, lentils and chickpeas are an excellent source of plant-based protein. Although legumes, with the exception of soybeans, are incomplete proteins, they can be combined with other foods such as rice to provide all essential amino acids.

# Plasma Proteins

The proteins present in the plasma of human blood are a mixture of simple proteins, glycoproteins, lipoproteins and other conjugated proteins are called “**Plasma Proteins**“.

# Types of Plasma Proteins:

The three major fractions of plasma proteins are known as **Albumin, globulin** and **Fibrinogen.**

- **Albumin** – 55.2%
- **α1-Globulin** – 5.3% (α1-Antitrypsin)
- **α2-Globulin** – 8.6% (ceruloplasmin)
- **β-Globulin** – 13.4% (β1-transferin)
- **¥-Globulin** – 11.0% (Antibodies)
- **Fibrinogen** – 6.5%

# Albumin:

- This is the most abundant class of plasma proteins. Albumin is synthesized in liver and consists of a single polypeptide chain.

- It is rich in some essential amino acids such as lysine, leucine, valine, phenylalanine, threonine, arginine and histidine. The acidic amino acids like aspartic acid and glutamic acid are also concentrated in albumin. The presence of these residues makes the molecule highly charged with positive and negative charge.

- Besides having a nutritive role, albumin acts as a transport carrier for various biomolecules such s fatty acids, trace elements and drugs.. Another important role of albumin is in the maintenance of osmotic pressure and fluid distribution between blood and tissues.

Low albumin levels are seen in a wide range of health problems, including diabetes, cancer, and liver disease, and are primarily a result of illness rather than a cause.

## Albumin and Ascites:

Ascites is a condition in which fluids accumulate between the membrane that lines the abdominal wall and the membrane that encompasses the internal organs (this space is called the peritoneal cavity). It usually occurs as a result of liver disease or cancer that has spread around the body.

Ascites has several possible causes, one of which is low albumin levels. Because there is less albumin in the blood to maintain the osmotic pressure inside the vessels, fluids diffuse out of vessels into the peritoneal cavity.

## Globulins:

### α1-Globulin:

This fraction includes several complex proteins containing carbohydrates and lipids. These includes α1-glycoprotein and α-lipoproteins.

Lipoproteins are soluble complexes which contain non-covalently bound lipid. These proteins act mainly as transport carrier to different types of lipids in the body.

## α2-Globulins:

This fraction also contains complex proteins such as α2-glycoproteins, prothrombin and ceruloplasmin (transports Cu).

Prothrombin plays an important role in blood clotting.

Ceruloplasmin is a glycoprotein synthesized in liver and is an important component of copper metabolism in the body. Nearly 95% of plasma copper is bound to this protein.

Abnormalities in ceruloplasmin synthesis have been associated with neurodegenerative disease. Low circulating serum ceruloplasmin levels served as a marker for Wilson's disease

Wilson disease is a rare autosomal recessive inherited disorder of copper metabolism that is characterized by excessive deposition of copper in the liver, brain, and other tissues. Hepatic dysfunction is the presenting feature in more than half of patients. Most patients have neuropsychiatric manifestations.

## β-Globulins:

This fraction of plasma proteins contains transferrin which transports non-heme iron in plasma.

Transferrin is an iron transport protein. In plasma it can be saturated even up to 33% with iron. It has a low content of carbohydrate.

The blood transferrin level is tested for diverse reasons: to determine the cause of anemia, to examine iron metabolism (for example, in iron deficiency anemia) and to determine the iron-carrying capacity of the blood.

Low transferrin can impair hemoglobin production (since to make hemoglobin, you have to have iron) and so lead to anemia. Low transferrin can be due to poor production of transferrin by the liver (where it's made) or excessive loss of transferrin through the kidneys into the urine. Many conditions including infection and malignancy can depress transferrin levels. The transferrin is abnormally high in iron deficiency anemia.

Liver makes transferrin. When your body's stores of iron run low, your liver produces more transferrin in order to get more iron into your blood.

## ¥-Globulins:

These are also called as Immunoglobulins and possess antibody activity. On the basis of their electrophoretic mobility they are classified as IgG, IgA and IgM.

## Fibrinogen:

It is a fibrous protein. Fibrinogen plays an important role in clothing of blood where it is converted to fibrin by thrombin.

# Functions of Plasma Proteins:

**1.Protein Nutrition:** Plasma proteins act as a source of protein for the tissues, whenever the need arises.

**2.Osmotic Pressure and water balance:** Plasma proteins exert an osmotic pressure of about 25 mm of Hg and therefore play an important role in maintaining a proper water balance between the tissues and blood. Plasma albumin is mainly responsible for this function. During the condition of protein loss from the body as occurs in kidney diseases, excessive amount of water moves to the tissues producing edema.

**3. Buffering action:** Plasma proteins help in maintaining the pH of the body.

**4- Transport of Lipids:** One of the most important functions of plasma proteins us to transport lipids and lipid soluble substances in the body.

**5- Transport of other substances:** In addition to lipids, plasma proteins also transport several metals and other substances a2-Globulins transport copper (Ceruloplasmin) and non-heme iron is transported by transferrin present in β-globulin fraction. Calcium, Magnesium, some drugs and dyes and several cations and anions are transported by plasma albumin.

**6- Blood Coagulation:** Prothrombin present in a2-globulin fraction and fibrinogen, participate in the blood clotting process.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